UNITED STATES PATENT AND TRADEMARK OFFICE

UNITED STATES DEPARTMENT OF COMMERCE
United States Patent and Trademark Office
Address: COMMISSIONER OF PATENTS AND TRADEMARKS
Washington, D.C. 20231
www.uspto.gov

APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/310,638	05/12/1999	HERMONA SOREQ	2391.00096	9102

7590 12/20/2002

JOHN P. WHITE
COOPER & DUNHAM LLP
1185 AVENUE OF THE AMERICAS
NEW YORK, NY 10036

EXAMINER	
CROUCH, DEBORAH	
ART UNIT	PAPER NUMBER
1632	

DATE MAILED: 12/20/2002

18

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application N .	Applicant(s)	
	09/310,638	SOREQ ET AL.	
	Examin r	Art Unit	
	Deborah Crouch, Ph.D.	1632	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *15 October 2002* .

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-24 and 26* is/are pending in the application.

4a) Of the above claim(s) *1-10,15,16,21 and 22* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *4,11,17-20,23,24 and 26* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☒ The drawing(s) filed on *May 12, 1999* is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

11)☐ The proposed drawing correction filed on _____ is: a)☐ approved b)☐ disapproved by the Examiner.

If approved, corrected drawings are required in reply to this Office action.

12)☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. §§ 119 and 120

13)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____ .

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

14)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application).

a) ☐ The translation of the foreign language provisional application has been received.

15)☒ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO-1449) Paper No(s) *3* .
4) ☐ Interview Summary (PTO-413) Paper No(s). _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other:

A request for continued examination under 37 CFR 1.114, including the fee set forth in 37 CFR 1.17(e), was filed in this application after final rejection. Since this application is eligible for continued examination under 37 CFR 1.114, and the fee set forth in 37 CFR 1.17(e) has been timely paid, the finality of the previous Office action has been withdrawn pursuant to 37 CFR 1.114. Applicant's submission filed on October 15, 2002 has been entered. The arguments contained therein have been fully considered but are not persuasive.

The PTO-1449, filed May 19, 2000, has been reviewed by the Examiner, where upon three references were found to only state the authors name, but lacking any other information. These references have been lined out as not complying with 37 CFR 1.97. A copy of the PTO-1449 is enclosed with this office action.

The terminal disclaimer filed on May 4, 2001 disclaiming the terminal portion of any patent granted on this application that would extend beyond the expiration date of U.S. Patent 5,932,780 has been reviewed and is accepted. The obviousness type double patenting rejection has been overcome.

The amendments to the claims have overcome the rejection made in the previous office action under 35 USC 112, second paragraph.

Claim Rejections - 35 U.S.C. § 112

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 11-14, 17-20, 23, 24 and 26 remain rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for transgenic mice and frog tadpoles whose genomes

comprise a transgene comprising a AChE promoter operatively linked to a DNA sequence encoding a splice variant of human AChE expressing AChE with acetylcholine esterase activity, wherein said sequence is expressed in cells of said mouse and where said mouse or tadpole exhibits changes in its neuromuscular junction structure, or and assay systems of said mouse or tadpole or transgenic nonhuman mammals whose genome comprises a DNA sequence encoding a splice variant of human AChE operably linked to a mammary gland promoter, where expression of the DNA sequence results in the production of detectable levels of enzymatically active AChE in the milk of the mammal, does not provide enablement for the preparation and use of transgenic animals comprising any and all variants of said cholinesterase genes or assay systems of these animals. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the invention commensurate in scope with these claims.

Applicant argues that the declaration by Dr. Hermona Soreq states that one of skill at the time of filing would have been able to prepare and use any transgenic animal comprising cholinesterase genes and variants thereof, use such transgenic animals as assay systems and use such transgenic animals for the production of HAChE in the milk produced by such animals. Please note that in view of Dr. Soreq's statements a scope has been made to a nonhuman mammal producing HAChE in its milk. The claims encompassing the bioreactor need to written such that the claimed animal has use as a producer of HAChE. As of now there is no promoter to direct mammary gland expression, which does not have to be a mammary gland specific promoter, or that the protein is produced or secreted into the milk of the mammal. As written the present claims do not have an enabled use.

However, with regard to the production of animal models for the study of the role of AChE in the development of the nervous system, more than mere expression is required for the claimed animals to have an enabled use. There needs to be some effect on the progenitor cells of the nervous system or the

outcome of nervous system development. The mere presence of the transgene in the cells of the animal is not going to have any effect at all on nervous system development.

Dr. Soreq states (parag. 4 (A)) that the specification provides guidance as to the making and using of transgenic animals comprising any and all variants of the cholinesterase genes or assay systems of these animals. Issue is taken with this statement as the animals to be used either as a bioreactor or an assay system must express the cholinesterase to some effective level. For a bioreactor the effective level would be detectable active enzyme in the milk. For the developmental model, some effect of overexpression on the nervous system. The present claims only require the animal to have the DNA sequence in its cells.

Dr. Soreq states (parag. 4 (B)) that cholinesterases neither require membrane structure or glycosylation for esterase activity. However, in view of the art references cited in the previous office action, which express conclusions opposition to declarant, more than a conclusionary statement is needed. Declarant needs to provide discussion or evidence as to why the references are incorrect.

Dr. Soreq states (parag. 4 (C)) that animals bearing variants of HAChE present a number of phenotypes beyond changes in neuromuscular junction structure. While the examiner has no issue with this statement, for the animals to be used as an assay, there must be some assayable phenotype. For Xenopus tadpoles and mice, as exemplified, the only common phenotype, at least as far as the examiner could find, is the changes in neuromuscular junction structure.

With regard to declarant's addition statements in parag. 5-8, the issues are the same. The specification discloses two types of animals, Xenopus tadpoles and mice, which show nervous system developmental abnormalities, and mice as a bioreactor. With regard to the mice and tadpoles as nervous system developmental models, more that mere expression is required. The specification provides no guidance as to how to use the animal models without an assayable endpoint. The art at the time of filing taught that the production of transgenic animals with any specific phenotype was unpredictable. With

regard to the bioreactor claims, such would be found allowable if crafted on the order of the scope rejection above. It is noted that the only bioreactor contemplated is a mammary/milk bioreactor.

All claims are drawn to the same invention claimed in the application prior to the entry of the submission under 37 CFR 1.114 and could have been finally rejected on the grounds and art of record in the next Office action if they had been entered in the application prior to entry under 37 CFR 1.114. Accordingly, **THIS ACTION IS MADE FINAL** even though it is a first action after the filing of a request for continued examination and the submission under 37 CFR 1.114. See MPEP § 706.07(b). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the mailing date of this final action.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Deborah Crouch, Ph.D. whose telephone number is 703-308-1126. The examiner can normally be reached on M-Th, 8:30 AM to 7:00 PM.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Deborah J. Reynolds can be reached on 703-305-4051. The fax phone numbers for the organization where this application or proceeding is assigned are 703-308-4242 for regular communications and 703-308-4242 for After Final communications.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the receptionist whose telephone number is 703-308-0196.

Deborah D. Crouch

Deborah Crouch, Ph.D.
Primary Examiner
Art Unit 1632

dc
December 19, 2002